(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on the batch for potency, moisture, pH, and identity.

(ii) Samples required: Five packages, each containing approximately 1.0 gram and one package containing approximately 2.5 grams.

(b) *Tests and methods of assay*—(1) *Potency.* Proceed as directed in § 436.300 of this chapter.

(2) [Reserved]

(3) *Moisture.* Proceed as directed in § 436.201 of this chapter.

(4) *pH.* Proceed as directed in § 436.202 of this chapter, using an aqueous solution containing 100 milligrams per milliliter.

(5) *Identity.* Proceed as directed in § 436.211 of this chapter, using the 0.5-percent potassium bromide disc prepared as described in paragraph (b)(1) of that section.

[39 FR 18976, May 30, 1974, as amended at 50 FR 19918, May 13, 1985]

§ 440.13a Sterile carbenicillin disodium.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Carbenicillin disodium is the disodium salt of α-carboxybenzylpenicillin. It is so purified and dried that:

(i) It contains not less than 770 micrograms of carbenicillin per milligram on an anhydrous basis. If it is packaged for dispensing, its carbenicillin content is not less than 90 percent and not more than 120 percent of the number of milligrams of carbenicillin that it is represented to contain.

(ii) It is sterile.

(iii) It is nonpyrogenic.

(iv) [Reserved]

(v) Its moisture content is not more than 6 percent.

(vi) Its pH in an aqueous solution containing 10 milligrams of carbenicillin per milliliter (or if packaged for dispensing, after reconstitution as directed in the labeling) is not less than 6.0 and not more than 8.0.

(vii) It gives a positive identity test for carbenicillin disodium.

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on the batch for potency, sterility, pyrogens, moisture, pH, and identity.

(ii) Samples required:

(*a*) If the batch is packaged for repacking or for use in the manufacture of another drug:

(*1*) For all tests except sterility: 10 packages, each containing approximately 300 milligrams; and 5 packages, each containing approximately 1 gram.

(*2*) For sterility testing: 20 packages, each containing approximately 300 milligrams.

(*b*) If the batch is packaged for dispensing:

(*1*) For all tests except sterility: A minimum of 15 immediate containers.

(*2*) For sterility testing: 20 immediate containers, collected at regular intervals throughout each filling operation.

(b) *Tests and methods of assay*—(1) *Potency.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Dissolve an accurately weighed sample in sufficient 1.0 percent potassium phosphate buffer, pH 6.0 (solution 1), to give a stock solution of convenient concentration; and also if it is packaged for dispensing, reconstitute as directed in the labeling. Then, using a suitable hypodermic needle and syringe, remove all of the withdrawable contents if it is represented as a single–dose container; or if the labeling specifies the amount of potency in a given volume of the resultant preparation, remove an accurately measured representative portion from each container. If it is a single dose container, use a separate needle and syringe for each container. Dilute with sufficient solution 1 to give a stock solution of convenient concentration. Further dilute the stock solution with solution 1 to the reference concentration of 20.0 micrograms of carbenicillin per milliliter (estimated).

(2) *Sterility.* Proceed as directed in §436.20 of this chapter, using the method described in paragraph (e)(1) of that section.

(3) *Pyrogens.* Proceed as directed in §436.32(b) of this chapter, using a solution containing 200 milligrams of carbenicillin per milliliter.

(4) [Reserved]

(5) *Moisture.* Proceed as directed in §436.201 of this chapter.

(6) *pH.* Proceed as directed in §436.202 of this chapter, using an aqueous solution containing 10 milligrams of carbenicillin per milliliter (or if packaged for dispensing, use a solution prepared as directed for reconstitution in the labeling).

(7) *Identity.* Proceed as directed in §436.211 of this chapter, using a 0.5 percent potassium bromide disc prepared as directed in paragraph (b)(1) of that section.

[39 FR 18976, May 30, 1974, as amended at 42 FR 59857, Nov. 22, 1977; 45 FR 22921, Apr. 4, 1980; 50 FR 19918, May 13, 1985; 51 FR 27532, Aug. 1, 1986]

§440.15 Cloxacillin sodium monohydrate.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Cloxacillin sodium is the monohydrate sodium salt of 5-methyl-3-(*o*- chlorophenyl)-4-isoxazolyl penicillin. It is so purified and dried that:

(i) Its potency is not less than 825 micrograms of cloxacillin per milligram.

(ii) [Reserved]

(iii) Its moisture content is not less than 3 percent and not more than 5 percent.

(iv) Its pH in an aqueous solution containing 10 milligrams per milliliter is not less than 4.5 nor more than 7.5.

(v) Its cloxacillin content is not less than 82.5 percent.

(vi) It passes the identity test.

(vii) It is crystalline.

(2) *Labeling.* It shall be labeled in accordance with the requirements of §432.5 of this subchapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of §431.1 of this subchapter, each such request shall contain:

(i) Results of tests and assays on the batch for potency, moisture, pH, cloxacillin content, identity, and crystallinity.

(ii) Samples required: 10 packages, each containing approximately 300 milligrams.

(b) *Tests and methods of assay*—(1) *Potency.* Use any of the following methods; however, the results obtained from the microbiological agar diffusion assay shall be conclusive.

(i) *Microbiological agar diffusion assay.* Proceed as directed in §436.105 of this chapter, preparing the sample for assay as follows: Dissolve an accurately weighed portion of the sample in sufficient 1 percent potassium phosphate buffer, pH 6.0 (solution 1), to give a stock solution of convenient concentration. Further dilute an aliquot of the stock solution with solution 1 to the reference concentration of 5 micrograms of cloxacillin per milliliter (estimated).

(ii) *Iodometric assay.* Proceed as directed in §436.204 of this subchapter.

(iii) *Hydroxylamine colorimetric assay.* Proceed as directed in §436.205 of this subchapter.

(2) [Reserved]

(3) *Moisture.* Proceed as directed in §436.201 of this subchapter.

(4) *pH.* Proceed as directed in §436.202 of this subchapter, using an aqueous solution containing 10 milligrams per milliliter.

(5) *Cloxacillin content.* Accurately weigh approximately 100 milligrams of the sample and dissolve in sufficient 5*N* sodium hydroxide to give a total volume of 25 milliliters. Place in a boiling water bath for 30 minutes. Cool, acidify 1 milliliter with 1 milliliter of dilute sulfuric acid (1 in 2), add 8 milliliters of water, and extract with two 25-milliliter portions of ethyl ether. Combine the ether extractives and extract with 25-milliliter portions of 0.1*N* sodium hydroxide. Combine the alkaline extractives and dilute to 100 milliliters with carbon dioxide-free water. Treat a portion of the cloxacillin working standard in the same manner. Using a suitable spectrophotometer, determine the absorbance of the solution in a 1-centimeter cell at the absorption peaks at 257±3 nanometers and at 282±3 nanometers compared with a reagent blank. Determine the percent